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DISSECTING ANEURYSM OF THE AORTA

A Review

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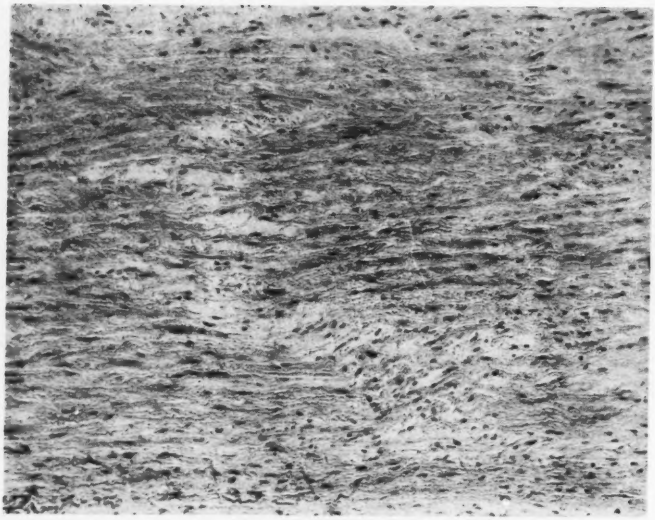
DISSECTING ANEURYSM OF THE AORTA is an intramural separation of the aortic wall by circulating blood that has penetrated and extended into the media. The process may arrest at this stage and heal, progress immediately, or extend at some later date. As the dissecting aneurysm progresses, it may rupture through the adventitia into the pericardial, pleural, or abdominal cavities and may obstruct arteries arising from the aorta. It may rupture back into the lumen and form a double-barreled aorta, which may persist, or the aneurysm may be filled with clot and subsequently heal, obliterating the secondary channel.

Etiology

Although the specific cause of the disease is not known, the lesion that generally is accepted as being precedent to dissecting aneurysm of the aorta is



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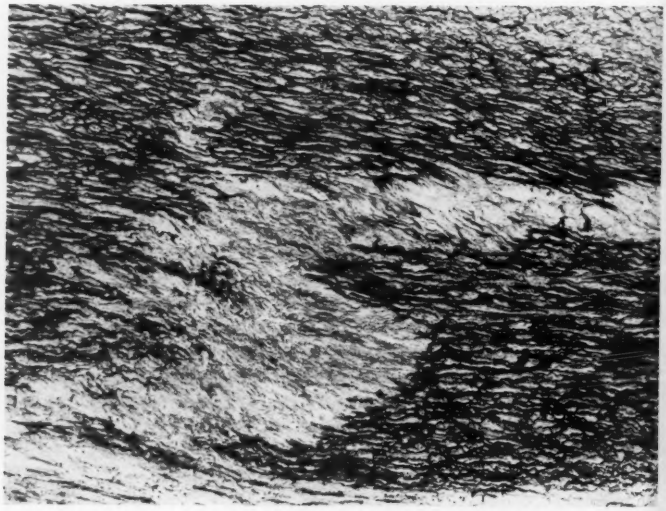

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Fig. 1. Changes in the media. (**A**) Medial degeneration (mucinous); hematoxylin, eosin and methylene blue stain, X80. (**B**) Marked loss of elastic tissue in a corresponding area; Verhoeff's stain, X80.

medial degeneration. This most often consists of mucoid changes in the media and focal loss of elastic tissue (Fig. 1); degeneration of muscle also may occur. The intimal rupture, almost universally present, may vary in size from a small defect a few millimeters in diameter to a large and nearly circumferential laceration. Some believe that the initial lesion may be hemorrhage into degenerated media derived from rupture of vasa vasorum. The originating point (Fig. 2) of dissection is predominantly in the ascending aorta, within a few centimeters of the aortic valve. It may occur in the regions of the ligamentum arteriosum and the left subclavian artery. The intramural dissection (Fig. 3) is of variable length and occurs mostly in the outer third of the media (Fig. 4), a circumstance permitting ready access to the adventitia and therefore possible rupture.

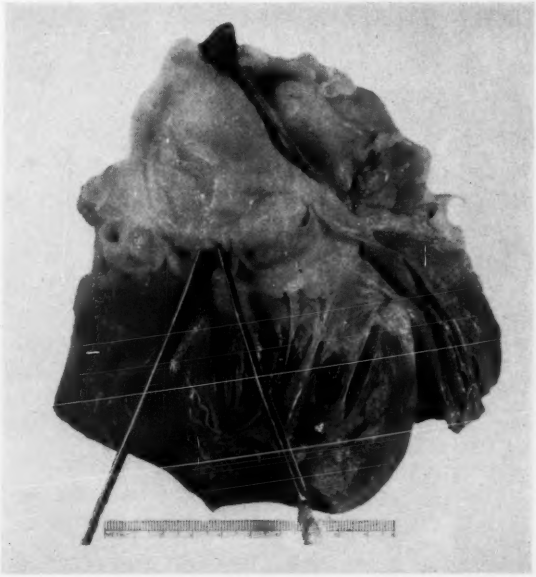


Fig. 2. Area of laceration of intima (marked by probes) at upper margin of aortic sinus.

The precedent disease and weakening of the media is of basic importance in the formation of dissecting aneurysm; however, no single feature may be responsible for all cases. Several factors are worthy of consideration regarding etiology.

Degenerative change. Degeneration of elastic tissue and other medial elements has been a common finding in dissecting aneurysm. Gore[1] has found that the deterioration of the elastic tissue is most common in those patients under 40 years of age. Erdheim[2] described a type of medial degeneration that he designated *medionecrosis aortae idiopathica cystica*, in which accumulations of

mucoid material were considered of primary importance. The significance of this finding is now generally recognized but it has not been observed constantly: Bauersfeld[3] found no cystic medionecrosis in a series of 15 dissecting aneurysms, and Glendy, Castleman, and White[4] found it in 6 of 13. Rottino[5] recognized it as being present but did not accept it as antecedent to the aortic medial degeneration he observed. In three completely studied cases, Moritz[6] found chromo-

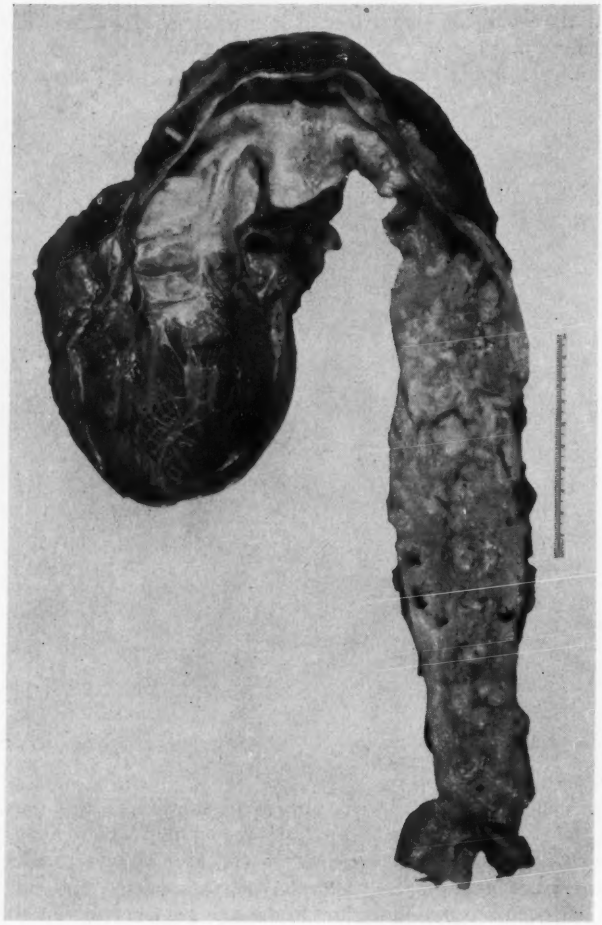
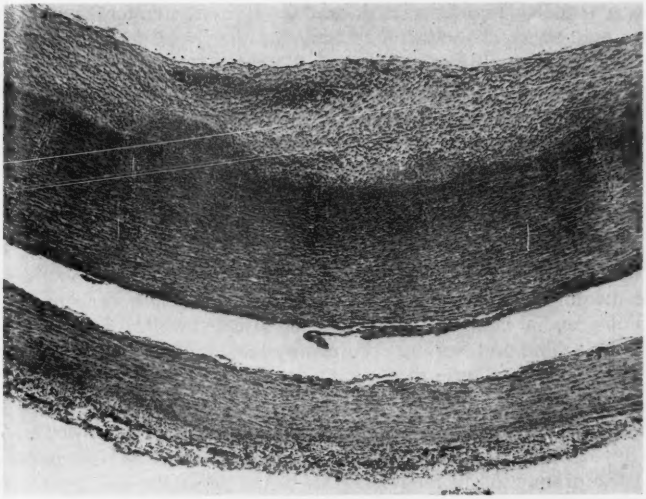


Fig. 3. Intramural dissection in aortic arch showing separation of vascular wall into two leaves. The dissecting aneurysm extended to the level of the diaphragm and had ruptured into the pericardium.



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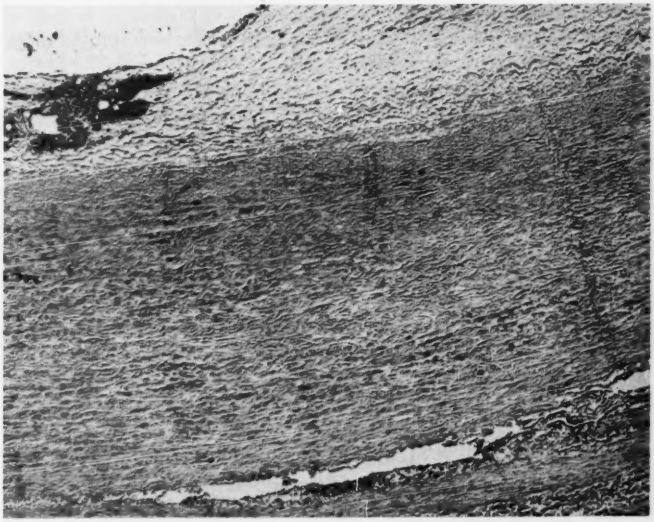

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Fig. 4. Channels of dissection. (**A**) Wide split near outer third of media; hematoxylin, eosin and methylene blue stain, X25. (**B**) Margin of channel in outermost media near adventitia. A focus of hemorrhage is present in the thickened intima; hematoxylin, eosin and methylene blue stain, X50.

tropic substance in the aortic media in all and, in addition, demonstrated it in the wall of the pulmonary artery in one. Mucinous change of a milder degree than observed in the dissecting aneurysms was found in 10 per cent of adult aortas and appeared to increase in intensity with advancing age. The underlying cause of medial degeneration is not known. Gore[1] has suggested that it may be a metabolic defect involving elastic tissue. Experimental evidence indicates that impairment of the blood supply to the aortic wall can lead to cystic degeneration as shown by Schlichter[7] who found definite cystic degenerative changes in the media of the aorta in dogs, one to six weeks old, after searing the adventitia.

Rottino[5] studied 12 cases of aortic dissecting aneurysm and found the medial degeneration to be characterized by loss of muscle, elastic tissue, and collagen. The medial changes predisposed to rupture of the vasa vasorum and the formation of a medial hematoma that split the diseased wall. An inflammatory reaction was lacking and healing occurred by loose scar formation and by regeneration of muscle and elastic tissue.

Amromin, Schlichter, and Solway[8] emphasized the importance of changes in the vasa vasorum, finding them sclerotic, hypertrophic, and narrowed in 7 of 12 cases. They believed that the resultant ischemia of the media is an important factor in the production of medionecrosis of the aorta. In seven cases of dissecting aneurysm of the aorta McCloskey and Chu[9] found alterations in the vasa vasorum consisting of medial hypertrophy and splitting of the internal elastic membrane of small arteries, medial hypertrophy with intimal proliferation and endothelial swelling of the arterioles, and endothelial swelling and proliferation of the capillaries.

Congenital anomalies. Coarctation of the aorta commonly is associated with medial degeneration of the aortic wall. Hamilton and Abbott[10] in a review of autopsy findings in 200 cases of coarctation of the aorta found that 16.5 per cent of the patients had died from aortic dissecting aneurysm. Schnitker and Bayer[11] reported that 31.9 per cent of 141 patients with dissecting aneurysm of the aorta, less than 40 years of age, had either true coarctation or definite narrowing of the aorta. A congenital bicuspid aortic valve may be found with dissecting aortic aneurysm. Gore[1] found this association in 9 of 32 patients less than 40 years of age.

Arachnodactyly also has been reported to predispose to dissecting aneurysm of the aorta.[12]

Hypertension. Hypertension usually is present in patients who develop dissecting aneurysm of the aorta, but many investigators regard it as of secondary importance. David, McPeak, Vivas-Salas, and White[13] found dissecting aneurysm of the aorta in 17 patients, all of whom had hypertension (blood pressure above 140/90 mm. Hg). Schnitker and Bayer[11] reviewed 580 case reports of patients having dissecting aneurysm and found the blood pressures often were not recorded, but of the 44 patients less than 40 years of age, on whom such determinations were made, only 50 per cent were hypertensive. It is doubtful that even an extremely high blood pressure could cause dissection of the aorta, inasmuch as Klotz and Simpson[14] found at autopsy that a pressure of more than 1000 mm. Hg was necessary to rupture an aorta.

Dissecting aneurysm of the aorta occurring in hypertensive patients during methonium therapy recently has been reported by Beaven and Murphy.[15] Necropsy findings in 44 hypertensive patients who died after methonium or pentolinium therapy showed that nine had dissecting aneurysm of the aorta, an incidence that the authors believed was beyond chance expectation. Of the 44 patients, 34 had malignant hypertension and 10 benign hypertension. Of the nine patients with dissecting aneurysm, six had had malignant hypertension and three benign hypertension. The authors suggested three possible explanations of this association: (1) Treatment prolonged life and allowed this complication to develop; (2) the fluctuations in the blood pressure encouraged the development of dissecting aneurysm; and (3) the hypotensive agents possibly had a specific biochemical effect on the aorta. Present experience suggests that the first of these explanations is probably the best.

Atherosclerosis. Atherosclerosis is present in the majority of cases of dissecting aneurysm of the aorta, but probably is of only minor etiologic importance inasmuch as it is such a common pathologic change in the aorta. Atherosclerosis is a disease primarily of the subintimal connective tissue and extends to involve the media adjacent to the intima, while a dissecting aneurysm involves primarily the outer portion of the medial layer. Bauersfeld[3] has observed that when intimal tears from a dissecting aneurysm are present in association with atherosclerosis they usually are found between two atherosclerotic plaques rather than in them. An intimal tear usually is located within the first few centimeters of the ascending aorta, an area less commonly involved with atherosclerotic plaques than is the rest of the aorta.

Pregnancy. In women less than 40 years of age there appears to be a distinct relationship between pregnancy and dissecting aneurysm of the aorta. Schnitker and Bayer[11] found that 35 per cent of the reported patients less than 40 years of age who had dissecting aneurysm of the aorta were women, and 49 per cent of those women were pregnant. In 20 women the dissection occurred antepartum, in 2 postpartum, and in only 2 at the time of labor.

Granulomatous giant-cell aortitis. Two cases of dissection with rupture of the aorta have occurred apparently as a direct complication of granulomatous giant-cell aortitis. Magarey[16] described a 75-year-old woman who allegedly was in good health prior to an unexpected and sudden death on a commode, and McMillan[17] described a 58-year-old man who died shortly after developing a left hemiparesis. Histologically in both instances medial changes were predominant and consisted of granulomatous reaction with giant-cell formation in the areas of destruction and an infiltration of lymphocytes and plasma cells. Giant cells formed a striking feature and were observed to be in close relation to fragments of elastic tissue.

Syphilis. Syphilis at one time had been suggested as a possible predisposing factor but is no longer so regarded. In their review of cases of dissecting aneurysm, Schnitker and Bayer[11] found only five (3.5 per cent) with a history of syphilis. Shennan[18] reported an incidence of 10 per cent in a series of 218 cases. Weiss[19] has pointed out that syphilitic aortitis tends to fuse the layers of the aorta, thereby actually hindering dissection. In Bauersfeld's[3] series of dissecting

aneurysms there were two cases with syphilitic involvement of the aorta, in each of which dissection, involving the ascending aorta, stopped at the beginning of the syphilitic aneurysm.

Incidence

The true incidence of dissecting aneurysm of the aorta is unknown. Only 30 cases were seen at the Massachusetts General Hospital in 49 years (1897 to 1946).[13] The incidence at autopsy is reported as about 1 in 500 cases. Regarding the age of the patients, the greatest frequency of dissecting aneurysm appears to be between the fifth and seventh decades of life; however, cases have been reported in which the age incidence ranged from 14 months to 100 years. Schnitker and Bayer[11] found that 24 per cent of their patients were less than 40 years of age. The sex ratio for occurrence of dissecting aneurysm is about 1 to 3 in favor of males.

Clinical Features

Symptoms. Pain is by far the most frequent symptom. It occurs suddenly and usually is severe from the onset. Patients describe it as sharp, burning, searing, or tearing. Usually it is not related to physical effort or activity and it is located in the anterior part of the chest, in the epigastrium, or frequently in both regions. Pain also may begin in or spread to the intercapsular region, neck, midback, flank, or sacrum, and occasionally it may extend into the upper or lower extremities.

Syncope may be the initial symptom but when the patient regains consciousness there usually is severe pain. A few cases have been reported in which syncope and pain were absent. The mechanism of syncope has been attributed to involvement of the depressor nerve endings in the aortic arch, and to cerebral ischemia secondary to pooling of large quantities of blood in the false passage of the aorta or, more commonly, to blockage or dissection of the innominate and common carotid arteries. Neurologic symptoms occur in about one half of the cases and symptoms of acute arterial insufficiency are frequent. Other symptoms may occur and include dyspnea, nausea, vomiting, orthopnea, oliguria, hemoptysis, ankle edema, melena, hematemesis, and hematuria.

Physical findings. There are few pathognomonic signs. Nissim[20] considers a reduplicated pulsation in an artery to be diagnostic. It is believed to be due to a difference in the rate of propagation of the pulse wave through the lumen of the involved artery because of its dissected coats. Shennan[18] has described a delay in conduction of the pulse beat, which he considers significant. In dissecting aneurysm of the aorta, the delay in the pulse beat when compared with the apical beat can occur in all arteries because of a weakening of the pressure of the blood stream passing through the involved aorta.

From the nature of dissecting aneurysm of the aorta it is easy to understand the lesser or greater involvement of various parts of the body. A patient having this condition usually is in acute distress and frequently appears to be in shock,

but the blood pressure is within normal limits or may be elevated. The pulse rate not infrequently is normal or slow and the temperature ranges between 99 and 103 degrees F. if the patient survives more than 48 hours.

Since most dissecting aneurysms begin in the ascending portion of the aorta, the heart may be involved in a variety of pathologic processes. Myocardial infarction may occur when there is obliteration of the coronary arteries by proximal extension of the dissection. Pericarditis occurs in approximately one third of the cases: it may result from an adventitial tear in the intrapericardial portion of the aorta, allowing a seepage of blood into the pericardial sac which may cause cardiac tamponade and death, or it may result from uremia if the dissecting aneurysm has occluded both renal arteries. Aortic insufficiency occurs in approximately 25 per cent of these patients. Cardiac enlargement from pre-existing hypertension usually is present.

Various pulmonary changes may occur when the dissection involves the thoracic aorta distal to the pericardial reflection. Pleural effusion is a relatively common finding and usually occurs on the left side. There are two explanations for its frequent occurrence on the left side: the aorta is in close proximity to the left pleural cavity and when there is rupture through the adventitia in this region it usually results in hemothorax; and dissection along the pulmonary artery may occur following the line of least resistance, which is along the left main pulmonary artery. Pulmonary congestion and atelectasis are frequent findings.

When neurologic manifestations are present they often facilitate the diagnosis. Involvement of the convex surface of the arch of the aorta may occlude the carotid artery and produce clinical symptoms resembling those of cerebrovascular accident—homolateral blindness with contralateral flaccid paralysis, hemianesthesia, and aphasia, called *carotid hemiplegia* by Weisman and Adams.[21]

Obstruction of the subclavian artery or arteries may result in ischemic necrosis of peripheral nerves, manifested by a pulseless, cold, weak extremity with anesthesia and loss of tendon reflexes. The changes often are temporary, lasting minutes to hours. Occlusion of an iliac artery may produce similar temporary symptoms in the lower extremity. Green and Saphir[22] reported a case in which the findings indicated an acute iliac occlusion, except for ecchymosis of the lower abdominal wall resulting from extension of the dissection into the deep inferior epigastric artery.

The intercostal, lumbar, and sacral arteries frequently are involved when the dissection spreads down the descending aorta. Occlusion of the ostia of the intercostal arteries in the lower thoracic and abdominal aorta may produce ischemic spinal necrosis or hemorrhagic infarction, resulting in flaccid paralysis and loss of sensation below the spinal level involved. Several factors determine whether the blood supply to the anterior spinal artery will be impaired. Anatomically the segmental arteries vary as to their site of origin from the posterior wall of the aorta. The dissection usually occurs on the anterior wall and extends in a spiral fashion. Weisman and Adams[21] noted that most of their cases with neurologic complications were in elderly patients in whom the circulation already had been impaired by atherosclerosis.

Tuohy, Boman, and Berdez[23] have stressed the diagnostic importance of wandering paralysis and vacillating sensory disturbances occurring below the level of the umbilicus.

Involvement of the mesenteric arteries may cause symptoms and signs that simulate an acute abdominal surgical emergency. There may be severe abdominal pain, hematemesis, melena, or signs of intestinal obstruction. Occlusion of the renal arteries usually results in infarction of one or of both kidneys. Symptoms of acute renal colic may be simulated and there may be albuminuria, hematuria, oliguria, or anuria, which result in a uremic death.

Laboratory findings. David and associates[13] stated that none of the electrocardiograms in their 17 cases of dissecting aneurysm of the aorta could be considered normal. Patterns of left ventricular strain and changes suggesting coronary disease predominated; the pattern of acute myocardial infarction was not found. The most common electrocardiographic pattern according to Levinson, Edmeades, and Griffith[24] is that of left ventricular hypertrophy. The pattern of myocardial infarction may occur when there is involvement of the dissecting process into the media of the coronary arteries, resulting in thrombosis and occlusion with myocardial infarction. The pattern of pericarditis may occur as the result of conditions previously described. Prolongation of Q-T intervals, sagging of RST segments, and T-wave flattening or inversion may occur as a result of electrolyte disturbances that are associated with uremia.

Leukocytosis usually is present. The white blood cell counts range from normal to 30,000 per cu. mm., with an increase in neutrophils. Anemia may result from bleeding into the aortic wall. Spinal fluid examination usually reveals clear fluid, but rarely it may be bloody from an associated spinal subarachnoid hemorrhage.

The most common finding on a thoracic roentgenogram is widening of the supracardiac shadow. This usually is progressive and involves the ascending or descending aorta. Occasionally a double-barreled shadow (especially on laminagrams) and areas indicating pleural effusion are seen. The angiocardiogram may be diagnostic, showing a dense concentration of the contrast medium in the main channel and a lateral or medial less dense concentration in the false channel.

Differential Diagnosis

Glendy, Castleman, and White[4] reported that myocardial infarction, embolism to some part of the body, and an acute abdominal surgical emergency are the conditions most likely to be confused with dissecting aneurysm of the aorta. Myocardial infarction is the most difficult to differentiate, but awareness of certain points may help to clarify the problem. In many cases of myocardial infarction, but rarely in cases of dissecting aneurysm, a history of angina is present. In myocardial infarction pain tends to develop gradually; in dissecting aneurysm pain is immediate and overwhelming. Radiation of pain down one or both arms occurs with myocardial infarction; whereas, with dissecting aneurysm radiation of pain is widespread to head, back, abdomen, and legs, but rarely to

arms. In addition, the persistence of hypertension, and obstruction of some part of the peripheral arterial circulation favors a diagnosis of dissecting aneurysm. Perhaps most important are the daily electrocardiograms that usually will confirm the diagnosis of myocardial infarction. Serum transaminase concentrations may provide further help in the differentiation.

Embolism to the aortic bifurcation, iliac, cerebral, or pulmonary arteries may be confused with dissecting aneurysm. The severe pain either in the chest or in the abdomen, with little if any dyspnea, the sudden onset of symptoms without evidence of previous heart disease or thrombophlebitis which might provide a source for embolism, and the usually uncontrollable course of the illness help to distinguish dissecting aneurysm in most instances.

An abdominal surgical emergency may be simulated by dissecting aneurysm when it involves the abdominal aorta. However, when dissecting aneurysm is present, the pain is likely to extend downward into both flanks. The presence of hypertension and the absence of previous symptoms related to the abdominal viscera or specifically to the kidneys indicate the possible presence of a dissecting aneurysm.

Levinson, Edmeades, and Griffith[24] state that the sudden appearance of an aortic diastolic murmur in a patient with hypertension who has severe chest pain is almost always pathognomonic of a dissecting aneurysm of the aorta. Various causes of the murmur have been cited. In Resnick and Keefer's[25] case, it appeared that the functional similarity of the false sac to an arteriovenous shunt and the regurgitation through the intimal tear above the aortic valve produced the murmur. At autopsy, an intimal opening was found just above the aortic valve. Hamman and Apperly[26] attribute the murmur to stretching or dilatation of the aortic ring. Levinson, Edmeades, and Griffith[24] believe that an intimal tear just at or above the aortic ring loosens the commissure and the corresponding cusp drops to a lower level within the ring. A hematoma at or above the aortic ring will distort it sufficiently to cause unequal closure of the valve leaflets. This murmur must be differentiated from that caused by a ruptured aortic valve cusp that is associated with tachycardia and previous cardiac damage from syphilis, rheumatic fever, or bacterial endocarditis. Thoracic pain and shock usually are absent in endocarditis.

Prognosis

Dissecting aneurysm of the aorta is associated with a high mortality. Approximately 25 per cent of the patients die within the first 48 hours after onset of symptoms. Half of the patients survive for 3 to 60 days; and the remaining 25 per cent of the patients may live, but usually sustain a second dissecting aneurysm that results in death. About 10 per cent of the latter group survive because the aneurysm ruptures farther down the aorta back into the lumen and forms a double-barreled aorta.

Treatment

Heretofore there has been no specific treatment for the disease. Treatment consisted mainly of supportive measures including bed rest, liberal use of morphine and oxygen, and blood transfusions in case of profound shock. Anticoagulant therapy is contraindicated.

Gurin, Bulmer, and Derby,[27] in 1935, surgically treated a dissecting aneurysm located in an iliac artery by excising the internal wall of the aneurysm at the distal point of advance. This procedure allowed the blood in the aneurysm to flow back into the true lumen, but the patient died from uremia. Other surgical attempts to repair dissections [28-31] have consisted of closure by suturing a ruptured dissecting abdominal aneurysm, and by fenestration of the internal wall of the aneurysm. Heretofore, all of the patients who were reported as surgically treated died postoperatively, either from uremia or from rupture of the aorta,[27,28,30] except those reported recently by DeBakey, Cooley, and Creech,[29] and Swann and Bradsher.[31] Four of DeBakey, Cooley, and Creech's six patients with dissecting aneurysm recovered completely. More recently they have reported[32] that 13 patients with dissecting aneurysm of the aorta have been treated surgically. Of the 13, 10 have survived operation and apparently have remained well up to one and one-half years postoperatively. Their technic included transection of the aorta as close to the origin of the dissection as possible, creating a re-entry of the false lumen into the true lumen proximally, and obliteration of the false lumen distally by suturing the inner and outer layers of the aorta around its full circumference. Occasionally in cases in which the dissection begins near the left subclavian artery, the proximal portion of the aneurysm, including the origin, is resected and replaced with a homograft. The distal portion is obliterated as described above. Swann and Bradsher[31] recently reported successful treatment of a patient with acute dissecting aneurysm of the thoracic aorta by fenestration of the internal wall of the aneurysm and external wrapping of the aorta with nylon cloth. The patient apparently was well six months after surgery.

Shaw[30] believes that the ideal mechanical solution of the problem of dissecting aneurysm involves repair of the primary tear in the proximal aorta as well as evacuation of blood and thrombus from the lumen of the aneurysm. To locate the tear and control the bleeding during repair are formidable problems, since the dissection usually starts in the region of or proximal to the great vessels of the aorta. Solution of the problems will be accomplished along with more accurate and early diagnosis and improved methods of controlling hypothermia and circulatory arrest.

Certainly, any patient who develops dissecting aneurysm of the aorta should be considered a vascular surgical emergency because of the serious mechanical problem it presents and the ultimately grave prognosis on conservative management.

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COBALT-60* TELETHERAPY FOR PALLIATION OF CARCINOMA OF THE THORACIC ESOPHAGUS

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CARCINOMA OF THE ESOPHAGUS presents a distressing problem in management. Despite the improvement in surgical and radiologic technics, only 2 to 3 per cent of patients having this disease survive for five years after the diagnosis. Since most cases are diagnosed only after esophageal obstruction has developed and the tumor has spread to involve regional or distant lymph nodes, the primary objective of treatment usually is palliative—relief of the esophageal obstruction.

Surgical resection or a bypassing procedure frequently has been performed for the relief of obstruction even when the disease is uncontrollable and despite a significant operative mortality in patients in the older age group.[1] The objective of treatment is to give the patients the satisfaction of being able to swallow during the remaining months of life. Without treatment these patients eventually may not be able to swallow even saliva. Other procedures have been employed with the hope of palliation—such as bougienage which temporarily dilates the obstruction but is painful and exposes the patient to the risk of perforation, and gastrostomy which permits nourishment of the patient but denies him the pleasure of eating—but they have been abandoned in most medical centers because of unsatisfactory results.

For the most part the results of palliative roentgen therapy heretofore have been disappointing. The inability to relieve the dysphagia may be attributable to many factors, physiologic, pathologic, and physical. The physiologic factors include the advanced age (average age, 62 years) and the poor nutritional status of the patient when he first is seen (average loss of weight since onset of symptoms, 26 pounds). The pathologic factor is the lack of consistent radiosensitivity of the tumor. Lesions involving the lower end of the esophagus frequently are adenocarcinomas that are inconstant in their response to irradiation. Lesions that involve only a short segment of the esophagus usually contain a considerable amount of fibrosis and respond poorly to irradiation; whereas, superficial spreading lesions that involve longer segments of the esophagus respond much better to irradiation.[2]

The physical factors that have hindered the effectiveness of irradiation of esophageal carcinomas include: depth of the lesion which may preclude an adequate dose for control of the tumor; secondary dermatologic and constitutional reactions that were not justified or desired in view of the expected poor result.

The radioactive material used in this study was supplied on authorization of the Atomic Energy Commission, Oak Ridge, Tennessee.

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Supervoltage irradiation has immeasurably aided the radiotherapist in delivering a more nearly cancerocidal dose to deeply lying tumors. In comparison with other types of irradiation, supervoltage irradiation has a "skin-sparing" effect and better dosage levels at the tumor site and causes fewer systemic reactions because of the smaller volume of irradiated tissue. The cobalt-60 teletherapy unit emits gamma radiation equivalent in energy and physical distribution in the body to that produced by a 3,000,000-volt roentgen-ray machine.

In some medical centers the results of palliative roentgen therapy have been rewarding. Nielsen,[3] for example, has reported complete or nearly complete abolition of obstructive symptoms in four fifths of his patients who were adequately treated with rotational therapy in the medium voltage range (200 to 250 kv.). Autopsy examinations of the patients treated by irradiation have revealed, in many instances, that the primary tumor had been completely eradicated and that death had been caused by distant metastases.[3,4]

Cobalt-60 teletherapy has been employed at the Cleveland Clinic since September 1954, and a rotational device for this unit has been used since September 1955. Twelve patients having carcinoma of the thoracic esophagus have been treated. (Cases of carcinoma of the cervical esophagus are not included in this report because these lesions constitute another and special therapeutic problem.) All 12 of our patients were referred by the Department of Thoracic Surgery because of either one or both of the following limitations to surgical therapy: (1) the presence of extensive lesions, (2) the patients were poor-risk candidates for surgery.

Postirradiation roentgen examination of the esophagus was made of only 7 of the 12 patients. Many of our patients reside at considerable distances from the Clinic and are unable to return for follow-up examinations; their follow-up care is being managed by their local physicians. In six of the seven patients whom we followed, palliation was gratifying, and in some of these a fairly normal mucosal pattern traversed the former site of the tumor. In the seventh patient of our series the disease progressed despite treatment.

Roentgen findings before and after cobalt-60 teletherapy in each of three patients are shown in Figures 1 through 3. The first patient (Fig. 1A) had an extensive squamous cell carcinoma of the mid-esophagus. Following cobalt-60 teletherapy the patient had no dysphagia and the esophagogram (Fig. 1B) appeared to be normal except for absence of peristalsis through the segment formerly occupied by the tumor. Nine months after treatment, the patient was asymptomatic. The second patient (Fig. 2A) had an undifferentiated carcinoma occupying the middle third of the esophagus, at the level of the aortic arch. Prior to treatment, the patient was unable to swallow solids. After treatment, dysphagia was relieved and the postirradiation roentgenogram showed no evidence of tumor (Fig. 2B). Nine months after completion of cobalt-60 teletherapy, biopsy showed only chronic esophagitis. No dysphagia was present when the patient was last examined, 17 months after the termination of the cobalt-60 teletherapy. The third patient had a squamous cell carcinoma that occupied the mid-third of the esophagus (Fig. 3A). After irradiation, the esophagogram (Fig. 3B) showed no evidence of tumor, although there was a constriction at the site formerly occupied by the neoplasm. The patient had no dysphagia at the time he was last examined, four months after termination of treatment.

Fig. 1. (**A**) Squamous cell carcinoma of the upper third of the esophagus. There is a long segment of esophagus that is diffusely infiltrated by tumor. (**B**) Postirradiation appearance of the esophagus: no demonstrable evidence of tumor.

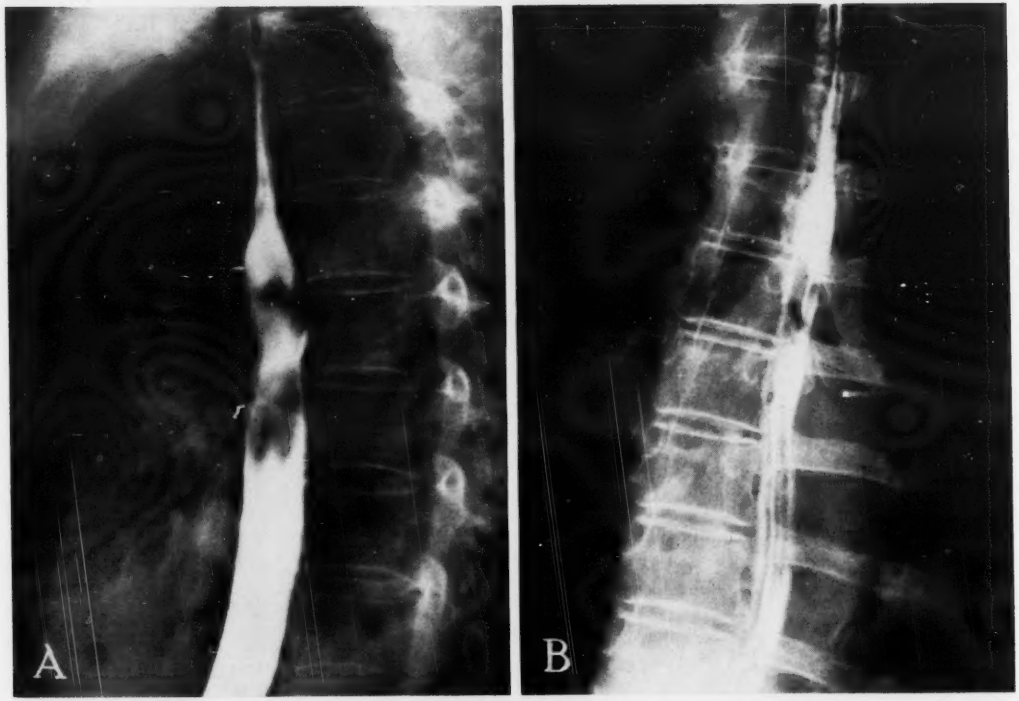

Fig. 2. (**A**) Tumor mass, occupying the mid-third of the esophagus, which proved to be an undiffereniated carcinoma. (**B**) Postirradiation: fairly normal mucosal pattern traverses the former site of the tumor.

fairly normal mucosal pattern traverses the former site of the tumor.

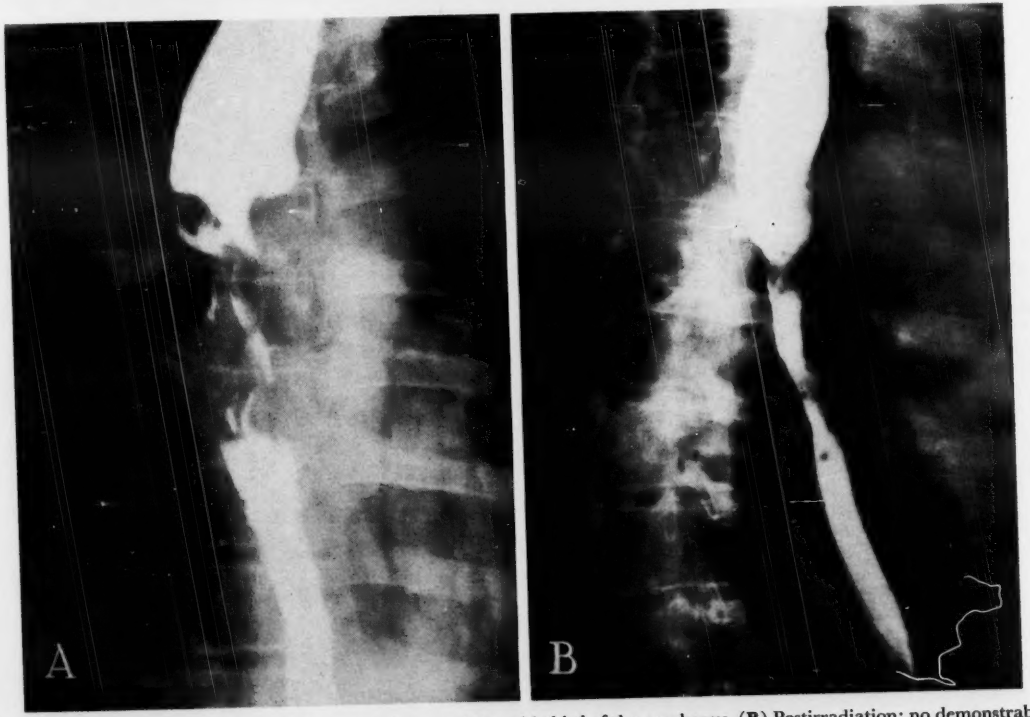

Fig. 3. (**A**) Diffusely infiltrating and constricting carcinoma of the mid-third of the esophagus. (**B**) Postirradiation: no demonstrable tumor, although a constriction is present at the former site of the tumor.

Summary and Conclusions

Palliation is the primary objective in the treatment of most patients with carcinoma of the thoracic esophagus. Cobalt-60 teletherapy has given encouraging results according to the follow-up findings in six of seven patients with carcinoma of the thoracic esophagus: it has brought about regression of the obstructing tumors without mortality and without significant morbidity. It is doubtful that cobalt-60 teletherapy or supervoltage roentgen-ray treatment using rotational technics will significantly increase the five-year survival rate of patients with carcinoma of the thoracic esophagus, but cobalt-60 teletherapy should be seriously considered for those patients in whom definitive resection is unwarranted or is not feasible.

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ANGIOGRAPHY OF THE CORONARY ARTERIES IN THE LIVE DOG

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IMPROVEMENTS in coronary angiography are basic to further advances in diagnosis and treatment of diseased coronary arteries. Exact localization of coronary occlusions by roentgen study must become possible if restorative surgical technics ever are to be utilized. Clinically, an ideal angiographic technic must be without hazard to the patient, must produce consistent visible filling of all three major branches of the coronary arteries, and must be reproducible. As yet, such standards of excellence have not been met.[1-4] It is the purpose of this paper to report our recent experience with angiography of the coronary arteries in healthy dogs.

Material and Method

Nine healthy mongrel dogs, each approximately 10 kg. in weight, comprised the series for our experiments. The dogs were anesthetized by intravenous injections of pentobarbital sodium (Nembutal sodium, Abbott). A no. 8 cardiac catheter, 50 cm. long, was inserted through one of the carotid arteries into the root of the aorta. The tip of the catheter was bent to make guidance possible. In one experiment the placement of the catheter was guided by fluoroscopy; in all others it was guided with the help of a continuous pressure-recording device†. The strength of the pulsations (as felt through the fingers of the operator) and the form of the curve of the pressure that was being recorded indicated whether the tip of the catheter was above, against, or had gone through the aortic valve. Strong pulsations transmitted through the catheter gave evidence that its tip had not accidentally entered the ostium of one of the coronary arteries.

Roentgenographic exposures were made after rapidly injecting all but 2 or 3 cc. of the contrast medium through the catheter. The roentgenograms were made at 1/60 second without regard to the phase of the cardiac cycle. Single films with each injection proved as satisfactory as multiple films taken by means of a hand-driven tray on which three films could be rapidly moved into position for exposure.

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†Sanborn one channel recorder, Sanborn amplifier, Stathem gauge.

Fig. 1. Injection of individual branches of coronary arteries in isolated dog heart. (**A**) The right coronary artery goes off high and in the dog is of small caliber. (**B**) The descending branch of the left coronary artery. (**C**) The circumflex branch of the left coronary artery. **B** and **C** are of large caliber.

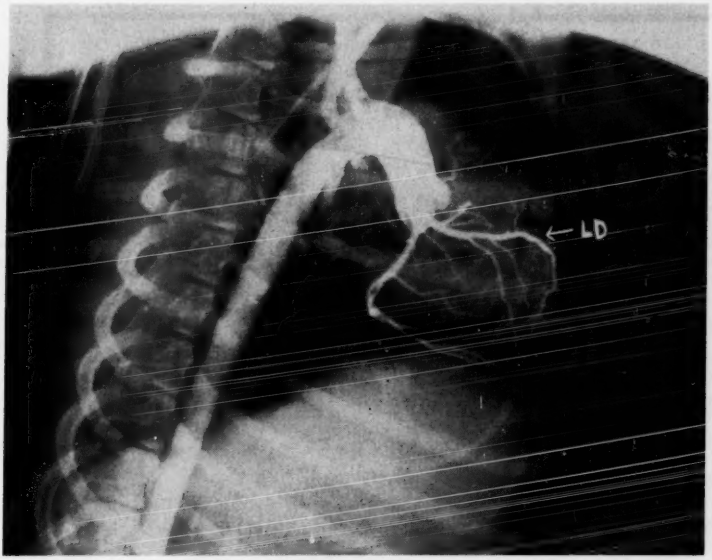

Fig. 2. Viewed with the dog in the right posterior oblique position; the right coronary artery originates from above the right sinus of Valsalva.

Ninety per cent Hypaque sodium* (sodium 3-5 diacetamido 2-4-6 triiodobenzoate) was used as the contrast medium. Thirty-three injections were given in the nine experiments. One dog received seven injections each of 10 cc. of 90 per cent Hypaque sodium without apparent ill effect. Ten cubic centimeters of 90 per cent Hypaque sodium per injection proved most satisfactory, which is approximately 1 cc. per kilogram of body weight. In two experiments Hypaque sodium was diluted with the dog's own blood in an unsuccessful attempt to obtain better filling of the coronary arteries. In one of these two experiments, 25 cc. of 90 per cent Hypaque sodium with 25 cc. of the dog's blood was given in one injection.

Results

None of the dogs died. All were allowed to survive until their wounds had healed. Experiment 2 was a complete failure because of the operator's inexperience in placing the catheter. In the other eight experiments delineation of the coronary arteries was obtained as follows: In all eight the descending branch of the left coronary artery was filled. In seven the circumflex branch of the left coronary artery was filled. In five experiments the right coronary artery was filled—although in two dogs it was hardly more than the entrance to the artery that was filled. Each of those two dogs was lying on its left side instead of in the

**Winthrop-Stearns, Inc., New York, New York.*

Fig. 3. (**A**) Viewed with the dog in the left posterior oblique position; the right coronary artery (R) originates higher than the left; the circumflex branch of the left (LC) tends to run parallel with the descending aorta; the descending branch of the left artery (LD) runs anteriorly. (**B**) Diagram of **A**.

left posterior oblique position; consequently, most of the right coronary artery was projected behind the aorta and was obscured by the contrast medium in it. In three experiments the right coronary arteries were not filled; two of those failures occurred when the Hypaque sodium was diluted with the dog's blood, and the third occurred when 5 cc. (instead of 10 cc.) of Hypaque sodium was injected.

Because in the living dog the coronary arteries are roentgenographically projected more or less over one another in one plane, we performed an experiment on an isolated heart by injecting the coronary arteries individually one by one (Fig. 1). The diameter of the right coronary artery of a dog usually is only one third of the diameter of that of either of the two main branches of the left coronary artery. Moreover, the right coronary artery originates from just above the right sinus of Valsalva (Fig. 2). The left coronary artery immediately divides into two branches of about equal size—the left circumflex and the left descending. If the common origin of these two branches is obscured by contrast medium in the root of the aorta, there is danger of misinterpreting one of those branches as being the right coronary artery. Awareness that the origin of the right coronary artery usually is above the sinus of Valsalva helps one to avoid such an error. The tip of the catheter should not lie in the posterior sinus of Valsalva, the only sinus from which or above which no coronary artery originates.

In this series the left posterior oblique position proved best for visualization and interpretation of all three coronary arteries on any single angiogram. In this position the left circumflex coronary artery tends to run parallel to the descending aorta and the vertebral column. The left descending coronary artery runs anteriorly. The right coronary artery can be seen to originate much higher than the left as a small, thin, tortuous shadow arising from above the sinus of Valsalva (Fig. 3).

Summary

The results of coronary angiography are presented, in which 90 per cent Hypaque sodium was used as the contrast medium in nine healthy dogs. Ten cubic centimeters of 90 per cent Hypaque sodium rapidly injected appears to be well tolerated by the healthy dog, and to provide good delineation of all three coronary arteries. The left posterior oblique position provided the best visualization. Aortic pressure recordings were used to help to determine the position of the catheter, as a safeguard against inserting the catheter into the coronary artery itself.

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AN IMPROVED METHOD FOR ENDOTRACHEAL INTUBATION DURING ANESTHESIA

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THE increasing use of endotracheal intubation during general anesthesia has made deficiencies apparent in the usual pattern of endotracheal catheters. For example, each of the numerous endotracheal tubes requires a correspondingly sized metal adapter for connection to the gas machine, and the adapter itself may be one of many shapes as well as types of slip-joint connectors. Whenever the adapter is placed within the endotracheal catheter, it reduces the size of the lumen of the catheter, causes turbulence in the gas flow and thereby increases resistance of the flow within the system. Currently used endotracheal catheters are made of rubber or heavy plastic. They are rather stiff and tend to kink when they are bent (Fig. 1a, a′). These nonpliable tubes predispose to sore throat and coughing and, also, through constant pressure cause ulceration and edema of the patient's anterior tracheal wall[1] and ulceration of the posterior laryngeal commissure. Furthermore, the continual rubbing of the rough catheter surfaces against these structures during respiratory movements, causes aggravation and occasionally granuloma formation.[2,3]

We have overcome these disadvantages by using a nonkinking endotracheal tube*, which at body temperature becomes pliable and adapts itself easily to the anatomic configuration of the upper respiratory tract (Fig. 1b, b′), yet which possesses the necessary rigidity for intubation. The tube is made of clear vinyl plastic of a high molecular weight. The method of construction is similar to that of a latex catheter. Each tube is individually molded on a form that is dipped into the coagulated vinyl plastic material. The tube is then heat-cured in much the same way as is latex rubber. This process gives the tube many of the characteristics of latex rubber, such as resistance to heat, pliability, and smoothness. However, it has an advantage over rubber: there is more body to it and, as a result, in relation to its wall thickness it can form a larger lumen. It can be autoclaved satisfactorily at 15-pound pressure for 15 minutes, but does not tolerate so much heat as does rubber. By the end of the 15-minute sterilizing period some of the plasticizer has evaporated and the tube may become too stiff.

This endotracheal tube will not easily kink; therefore, when the tube emerges from the mouth or the nose it may be bent to conform to the contour of the face without compromising the airway (Fig. 2). The length is appropriate for connection to the gas machine at a point distant from the mouth or nose and yet the dead space is not increased over that of the usual connections. The flare end of the tube permits adaptation directly to the Y Adapter or to the Adams Adapter, and eliminates need for any slip-joint adapters.

Manufactured by C. R. Bard, Inc., Summit, New Jersey.

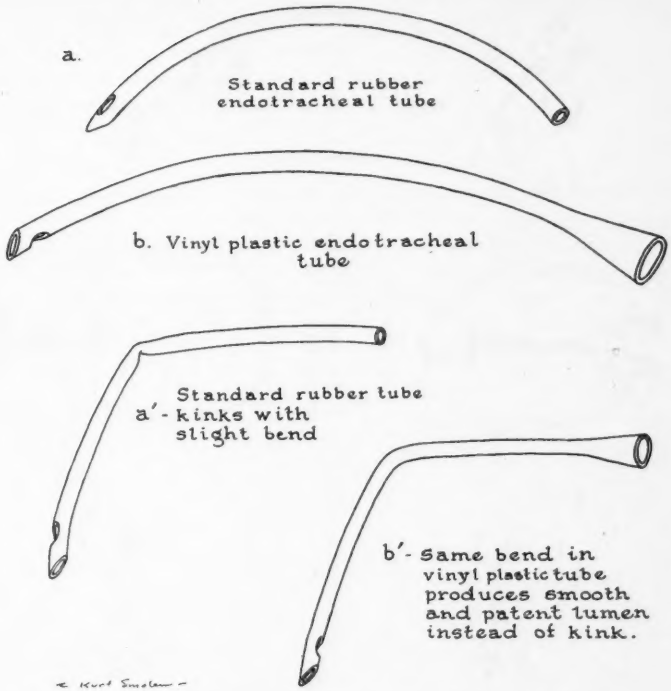
a.
Standard rubber endotracheal tube
b. Vinyl plastic endotracheal tube
Standard rubber tube
a'- kinks with slight bend
b'- Same bend in vinyl plastic tube produces smooth and patent lumen instead of kink.

Fig. 1. (a) Standard endotracheal tube with molded curve. Adapters and slip-joint connectors are required to close the anesthetic system. (a′) Standard endotracheal tube kinks, and occludes the lumen when bent. (b) Vinyl plastic tube has a flare end for direct connection to Y or Adams Adapters. (b′) Vinyl plastic tube is resistant to kinking when bent.

We have used this vinyl plastic type of tube for the past year in more than 3000 cases. Originally it was designed to satisfy requirements in surgery of the head and the neck, but its numerous advantages became so apparent that now it is used generally in all types of surgery requiring endotracheal intubation (Fig. 3). The advantages of the tube are apparent: 1. Decreased bulk upon the face of the intubated patient; this is ideal for surgery about the head and the face. 2. Smooth surface and pliability of the tube. At body temperature the endotracheal tube becomes readily pliable and will adapt itself to the anatomic conformity of the upper respiratory tract. This helps to eliminate pressure points and decreases the irritation to the larynx and tracheal mucous membrane. 3. The lumen of the endotracheal tube is not reduced by the insertion of slip-joint connectors. The flare end adapts directly to the Y and the Adams Adapter of the circle-system. In most cases the lumen of this connection is much greater than the lumen of the endotracheal tube.

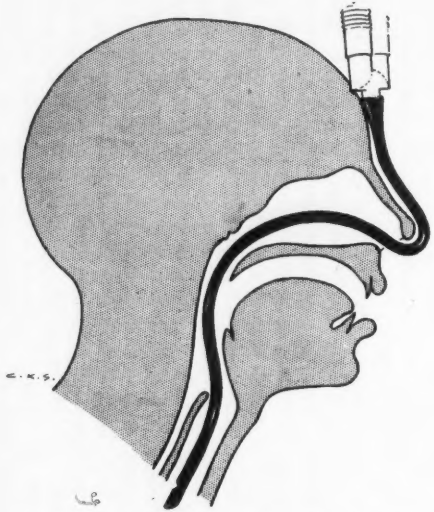

Fig. 2. The vinyl plastic tube introduced into the trachea via the nasal route and adapted directly to the Adams Adapter.

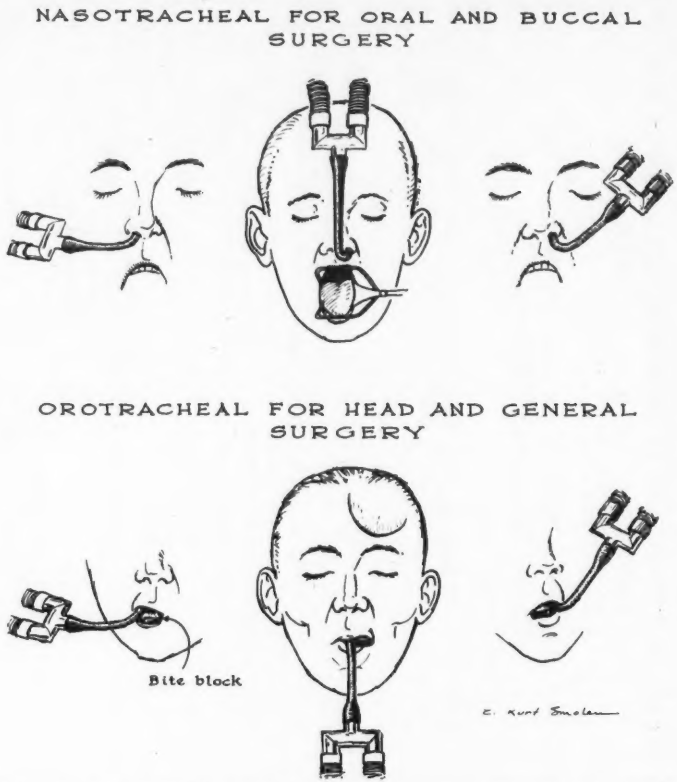

Fig. 3. Possible adaptations of the vinyl plastic tube for endotracheal intubation.

Summary

An improved, nonkinkable, vinyl plastic endotracheal tube is described which has the advantages of uniform pliability and rigidity, and direct adaptation to the gas machine, eliminating use of connectors.

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Fig. 3. Possible adaptations of the vinyl plastic tube for endotracheal intubation.

MALIGNANT SYNOVIOMA

Report of Two Unusual Cases

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MALIGNANT SYNOVIOMA is a well-recognized clinical entity as evidenced by the review of 222 cases by Tillotson, McDonald, and Janes[1] in 1951, and by other series subsequently reported. We are presenting two noteworthy cases: one in which the biologic behavior of the tumor was remarkable and the patient survived an exceptionally long time; the other in which the tumor arose in the anterior portion of the neck, a region not previously reported as a site of malignant synovioma.

Case Reports

Case 1. A 32-year-old white woman was admitted to the Cleveland Clinic Hospital on March 23, 1925, because of pain, swelling, and local discoloration behind the left knee. The symptoms had been present for 15 years, but during the few months before admission had gradually increased in severity.

Physical examination revealed a firm ovoid tumor mass in the popliteal space, which apparently was attached to underlying tissues but not to skin. The overlying skin showed slight bluish discoloration. There was no roentgen evidence of bony change or soft-tissue calcification. The tumor was removed on April 20, 1925, 28 days after admission.

The surgical specimen was a lobulated, soft, pale-gray, poorly encapsulated mass, 12 by 7 by 6 cm.; on bisection the cut surface was grayish white, homogeneous, friable, and moderately vascular. A review of the sections revealed the cell architecture to be typically that of malignant synovioma but with a pronounced epithelial appearance of the cells forming lumina (Fig. 1A). The irregularly shaped spaces were numerous and lined by prominent, cuboidal-to-columnar, pale-staining epithelial cells with uniformly small nuclei. Between these spaces were numerous small dark-staining spindle cells with occasional mitotic figures. No calcification was noted.

Irradiation was administered to the patient postoperatively.

The patient subsequently was seen three times at the tumor clinic of St. Vincent's Charity Hospital in Cleveland, Ohio, in 1938 (13 years postoperatively), 1947, and 1951. Each time there was removed from the popliteal space a small recurrent mass with the same histopathologic characteristics as those of the original tumor (Fig. 1B). In 1953, 28 years after excision of the original neoplasm, the patient still was living without evidence of distant metastasis.

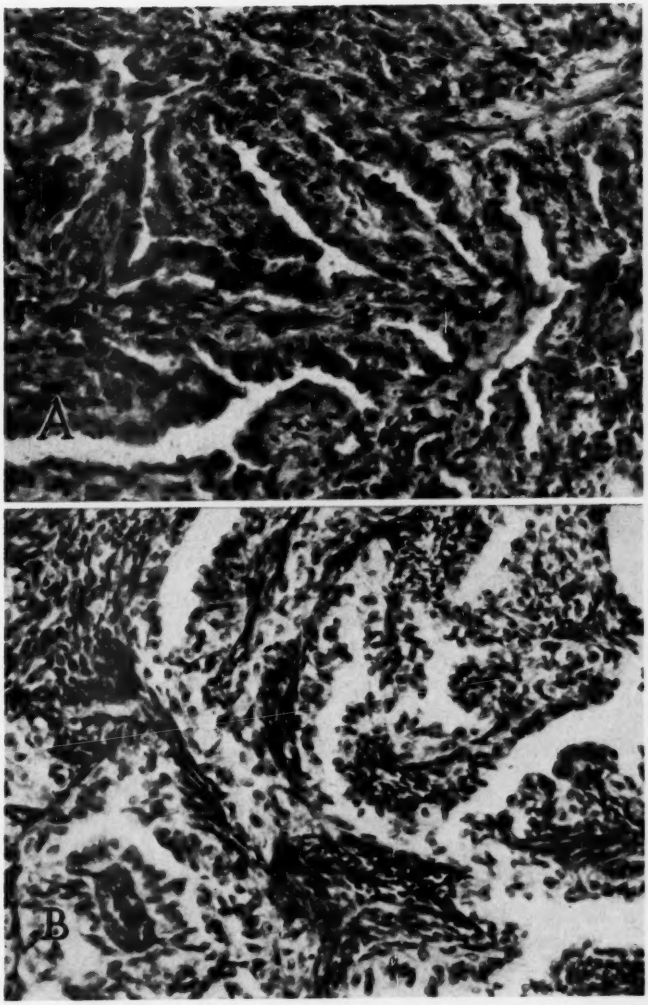

Fig. 1. Case 1. (**A**) Celloidin section of original tumor removed in 1925. The epithelial component is prominent. Hematoxylin and eosin; X270. (**B**) Recurrence removed in 1951. Hematoxylin and eosin; X270.

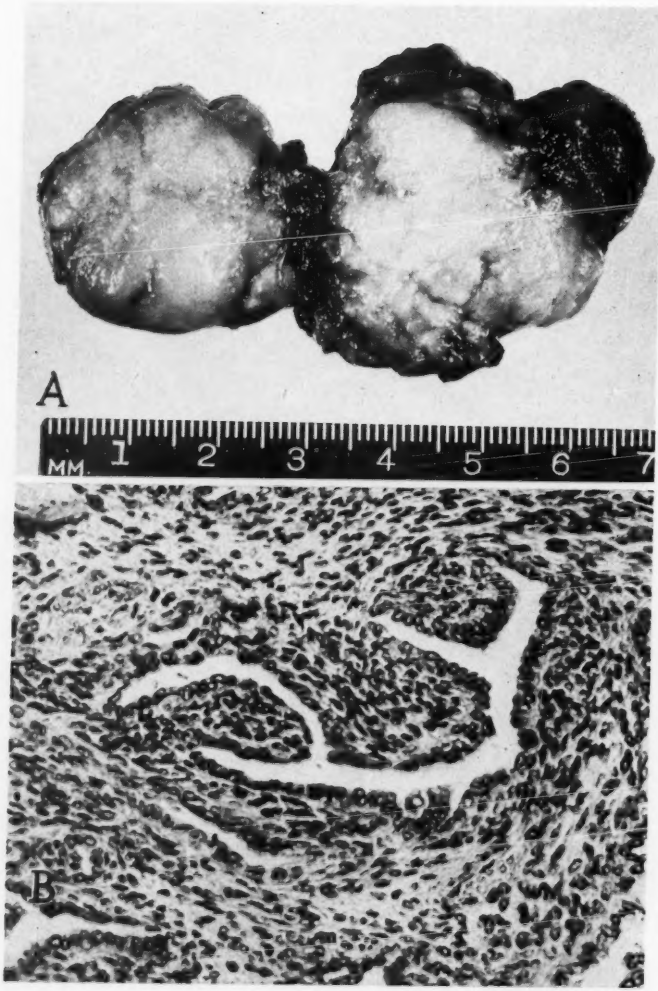

Fig. 2. Case 2. (**A**) Cut surface of bilobate gross specimen surgically removed. (**B**) Histology of neoplasm. The spindle-celled component is more loosely arranged in this area. Hematoxylin-eosin—methylene blue; X270.

Case 2. A 36-year-old white man was admitted to Cleveland Clinic Hospital on April 6, 1953, because of a mass in the left side of the neck. He stated that two years previously, after a severe upper respiratory infection, he had first noted a swelling in the left side of the neck under the jaw, which had reached its present size in a few weeks and then had remained stationary. Two months before admission he noted a persistent second swelling under the chin near the first mass. It seemed to him that the masses had fluctuated in consistence from soft to "stony hard."

Physical examination revealed the presence of two soft masses in the neck. The posterior tumor was located in the region of the left submaxillary gland; the anterior tumor extended under the tongue on the left side. On frozen-section examination the diagnosis was papillary carcinoma or malignant synovioma. Both masses were immediately excised in continuity.

The tissue that was removed was a bilobate mass, weighing 30.0 gm. (Fig. 2A). Each of the two lobes was firmly attached to a segment of the hyoid bone, 1.0 cm. in length. Both were covered by a thin capsule. The larger lobe measured 3.5 cm. in diameter, the smaller, 3.0 cm. On section, they were generally similar, being composed of soft, finely granular, gray-white tissue, and joined by a narrow isthmus of similar tumor. In addition, the larger lobe had a peripheral margin, 1 cm. in thickness, formed of dark-purple soft tissue.

The tissue was of the same histologic structure throughout the lobes and the isthmus. There were large, irregularly shaped spaces lined by cuboidal cells that occasionally formed papillary projections into the lumina (Fig. 2B). The intervening tissue was formed by dark-staining, small, spindle cells. In some areas these spindle cells were closely packed, and in others they were more loosely arranged. Occasional mitotic figures were present, and psammous calcification was noted in one area. The masses were covered by condensations of fibrous tissue, adjoined by skeletal muscle.

The patient has survived three years, and at the present time there is no evidence of local recurrence or metastasis.

Comment

Five-year survival rates in patients having malignant synovioma usually are less than 10 per cent; however, Pack and Ariel[2] reported a five-year survival rate of 19.1 per cent in their series. Stout[3] believes that malignant synovioma should be considered cured only when a patient remains well for at least ten years after treatment. No patient in his series survived for ten years, although one remained well for nine years after amputation and then died of pulmonary metastases before the ten-year period ended.

In our first patient the lesion manifested itself only by three local recurrences during a 28-year period, although histopathologically it was indistinguishable from the usual highly malignant form. One of Tillotson, McDonald, and Janes's[1] patients (case 23) who received contact irradiation in addition to surgery had a somewhat similar history—he had a local recurrence 13 years after therapy and was surviving 21 years after the original treatment.

Only five cases heretofore have been reported as occurring in locations other than the extremities. One malignant synovioma was described by Stout[3] as arising from the back of the neck, one by Eisenberg and Horn[4] from the anterior

chest wall, one by Wright[5] from the lumbosacral area, and two by Pack and Ariel[2] from the anterior abdominal wall. In our second patient the neoplasm arose retromandibularly in the upper cervical area.

Summary

Two unusual cases of malignant synovioma are reported. In one, the patient's survival after initial treatment (28 years) has been exceptionally long, and in the other, the tumor arose in the anterior portion of the neck, a site of origin not previously ascribed to this neoplasm.

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NISENTIL HYDROCHLORIDE ANALGESIA AND PENTOTHAL SODIUM AMNESIA IN DENTAL SURGERY

Preliminary Report

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and

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FEAR of even the simplest dental extraction under local anesthesia induces in many patients a state of anxiety which must be controlled to render them calm, relaxed, and co-operative for the surgical procedure. We recently initiated a clinical study of analgesia and amnesia for dental extractions in ambulatory patients in whom analgesia was produced by Nisentil hydrochloride (alphaprodine hydrochloride, Hoffmann-LaRoche) and amnesia by Pentothal sodium (thiopental sodium, Abbott). Nisentil hydrochloride has been used widely in obstetrics,[1] urologic examinations,[2,3,4] endoscopic procedures,[5] and oral surgery.[4,6]

This preliminary report presents our experience with Nisentil hydrochloride and Pentothal sodium in 128 cases requiring dental surgery.

An ideal analgesic for dental extraction (1) permits rapid induction, (2) effectively relieves pain, (3) does not interfere with the patient's ability to cooperate during the procedure, (4) has a total action not significantly longer than the operating time, and (5) causes a minimum of side reactions. Nisentil hydrochloride appeared to have most of these characteristics and it was chosen for our clinical studies in dental surgical procedures.

Alphaprodine hydrochloride. The use of alphaprodine hydrochloride was first reported by Ziering and Lee, in 1947.[7] Its chemical structure is similiar to that of meperidine (Demerol hydrochloride)—a synthetic piperidine derivative—but not to that of morphine. In a comparative study of Nisentil hydrochloride and morphine, in which equally potent analgesic doses of the two agents were given to normal volunteers, Gross, Holland, and Schueler[8] found that Nisentil hydrochloride had a more rapid onset of action, a shorter period of effectiveness, and fewer side reactions. Particularly notable was the relative infrequency of such side effects as nausea, vomiting, itching, and deep sedation.[9] In our study, two patients vomited postoperatively and four others complained of nausea. Dizziness, and diaphoresis occurred with greater frequency. The rapid effect and relatively short period of action of the drug permit considerable flexibility in administration. After intravenous administration, maximum effects are

obtained within three minutes, and the effects subsequently disappear within 30 to 60 minutes.[10] The sedative effect is very mild, and does not correspond to the depth of analgesia. Nisentil hydrochloride decreases the respiratory rate and tidal volume,[11] an effect that becomes pronounced when Pentothal sodium is used concomitantly. Therefore, to assure adequate alveolar ventilation, the patient is encouraged to take frequent deep breaths during the operative procedure.

Gruber, Lee, and Gruber[12] found that toxic doses of alphaprodine hydrochloride in rats, mice, and rabbits were evidenced by clonic convulsions and exophthalmos. Some animals died of respiratory failure.

Procedure

In the present study, 128 patients ranging in age from 8 to 71 years comprised the series. For each patient, routine history taking and physical examination preceded the operation. Premedication consisted of 50 to 100 mg. of Seconal sodium administered orally 45 to 60 minutes before operation. Upon his arrival to the dental chair, the patient's blood pressure, pulse, and respiratory rate were obtained and recorded. Five per cent dextrose in water was intravenously administered and with it was given 10 to 40 mg. of Nisentil hydrochloride. The dose is determined according to the patient's age, weight, and condition of general health. Dosage schedules for normal adults, excluding undernourished or obese patients, were calculated on the basis of 0.5 mg. per kg. of body weight. Average dosage for the normal adult female was 30 mg. and for the normal adult male 35 to 40 mg. Dosages for children may be determined by Young's rule[13]:

$$\text{Children's dose} = \frac{\text{Age times adult dose}}{\text{Age plus 12}}.$$

In the event of overdosage, Nalline hydrochloride[10] or Levallorphan tartrate[14] are effective antidotes. It is assumed, however, that provision for artificial respiration with oxygen by an anesthesia machine and endotracheal equipment under the supervision of a competent anesthetist are available. Three to five minutes after the Nisentil hydrochloride was given, 20 to 40 mg. (1 or 2 ml. of a 2 per cent solution) of Pentothal sodium was administered. Local anesthesia was used as a supplement in approximately 75 per cent of the cases. It should be emphasized, however, that the local anesthetic was infiltrated only into the gingival tissues, no attempt being made to achieve subperiosteal infiltration or nerve-conduction analgesia. Surgical procedures were then started and additional 20-mg. doses of Pentothal sodium were given as necessary. The patient remained conscious and awake, but drowsy, so he was able to respond to commands and to co-operate during the surgical procedure. Care was taken not to give an overdose of Pentothal sodium which would produce unconsciousness and lessen the safety of this technic. Apnea and unconsciousness occurred in six cases. These patients were in the older age group and were debilitated. Oxygen delivered by mask with positive-pressure breathing for approximately two minutes corrected this condition.

As mentioned before, close attention was paid to respiration, and the patient

was requested to breathe deeply. Upon completion of the procedure, the patient, still with his senses somewhat dulled, walked with assistance to the recovery room and was allowed to lie down. He reclined for 30 to 60 minutes, depending upon the extent of the procedure and the amounts of the anesthetic agents used and, when dismissed, he was placed in the charge of the person who had accompanied him to the Clinic.

Comment

The problems of anxiety and pain, and the need for anesthesia are related in dental surgery. Reassurance, sedation, intravenous anesthesia, and local block all contribute to the solution of these problems, and Nisentil hydrochloride seems to be a useful agent in producing these effects.

During the study of this method, it was observed that: (1) The patient is rendered analgesic but does not lose consciousness. (2) He remains co-operative, and follows instruction when asked to open his mouth or to turn his head from side to side. He breathes deeply upon request. (3) He retains his swallowing and coughing reflexes. (4) He seldom, if ever, experiences any pain where the needle is inserted and the anesthetic solution has infiltrated. (5) Amnesia for the surgical procedure is produced in approximately 80 per cent of the cases. A few patients cry out and manifest the facial grimacing ordinarily associated with reaction to pain but, later, after the operation has been completed, they will state that they have no memory of having pain. The release of emotional tension was observed in a few patients who simultaneously quietly cried and smiled when told that the operation had been completed. Failure to produce amnesia and analgesia was observed in 5 per cent of the cases. (6) The Pentothal sodium requirement with Nisentil hydrochloride is definitely reduced as compared with the amount required when Pentothal sodium is used by itself. In our series, the amount averaged about 100 mg. of Pentothal sodium per patient. On the basis of reports[15] from other oral surgeons it is estimated that at least 200 mg. or more of Pentothal sodium alone is required for the average dental surgical case. (7) In the majority of cases there is no postoperative pain. Narcotic addiction seems unlikely as a result of the method reported, as the patient receives but a single injection of Nisentil hydrochloride.

Summary

A technic for establishing a modified analgesic state suitable for ambulatory patients who are to undergo dental surgery is being studied. Nisentil hydrochloride, a relatively new basal analgesic, has been used in combination with premedication and Pentothal sodium amnesia. Properly employed, it plays a valuable role in relieving anxiety and pain, and as a supplement to local block. In selected cases this technic may be used for more extensive dental surgery that otherwise would require hospitalization and endotracheal anesthesia. This technic causes little or no interference with the homeostatic mechanisms of the patient during and after operation.

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AN IMPROVED METHOD OF ADJUSTING COMMERCIAL COLLOIDAL GOLD SOLUTION USED IN THE SERUM COLLOIDAL GOLD TEST

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THE precipitation of serum colloidal gold by human serum has been reported to be due to the presence of serum gamma globulin.[1,2,3] The serum colloidal gold test, when correlated with other clinical and laboratory findings, has proved of particular value in our institution as an aid to the diagnosis of struma lymphomatosa (Hashimoto's disease).[3,4] Its use in this disease was first reported by Cooke and Wilder,[5] and further discussed by Luxton and Cooke[6] more recently. Although electrophoretic analysis of the serum proteins is the most accurate quantitative measure of an increase in serum gamma globulin, its use is limited to a few large medical centers.

The widespread use of the serum colloidal gold test has been limited by the basic difficulty of adjusting the pH of commercial colloidal gold solutions. The purpose of this report is to present the details of an improved method of adjustment of commercial Lange's colloidal gold solution*, and to review the method of performing the test which is a slight modification of that described by Maclagan.[7]

Method of Adjusting Lange's Colloidal Gold Solution For Use in the Serum Colloidal Gold Test

A. Materials Required

1-a. Lange's colloidal gold solution

2-a. Normal serum

3-a. Positive serum

4-a. One per cent acetic acid solution

5-a. Barbital buffer solution, pH 7.6

Formula:		
Diethylbarbituric acid . . .	0.55	gm.
Sodium barbitone	0.31	gm.
Phenol	0.2	gm.
Distilled water	100	ml.

6-a. Test tube racks

**Lange's Colloidal Gold Solution, manufactured by Magar Chemicals, Inc., Cornwall Landing, New York; and by The Keystone Laboratory, Erie, Pennsylvania.*

7-a. Clean test tubes, 13 mm. by 100 mm.

8-a. Graduated serologic pipets, 5 ml., 1 ml., and 0.1 ml.

B. First Step

1-b. Arrange two rows each of eight test tubes in a rack, and number the tubes in each row *1* through *8*, from left to right.

2-b. Into each tube of the first row, pipet 0.02 ml. of the normal serum.

3-b. Into each tube of the second row, pipet 0.02 ml. of the positive serum.

4-b. To each tube of both rows, add 0.18 ml. of barbital buffer.

C. Acidification of the Colloidal Gold Solution

1-c. Arrange a third row of eight test tubes in another rack, and number the *tubes 1* through *8*, from left to right.

2-c. Deliver to the bottom of each tube, beginning at the left with *tube 1*, the following amount of 1 per cent acetic acid solution, in respective order: 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08 ml.

3-c. To each tube, add 4 ml. of colloidal gold solution and mix. *Tube 1* now contains 0.0025 ml.; *tube 2*, 0.005 ml.; *tube 3*, 0.0075 ml.; *tube 4*, 0.01 ml.; *tube 5*, 0.0125 ml.; *tube 6*, 0.015 ml.; *tube 7*, 0.0175 ml.; and *tube 8*, 0.02 ml. of 1 per cent acetic acid per ml. of colloidal gold solution.

D. Determination of the Optimal Quantity of Acid for the Test

1-d. Using a graduated pipet, add 1 ml. of acidified gold solution from *tube 1* (*3-c*) to each of *tubes 1* (*4-b*) of the positive and negative serums. Similarly pipet 1 ml. of acidified gold solution from *tube 2* (*3-c*) to each of *tubes 2* (*4-b*) of the positive and negative serums. Continue this process for the remainder of the correspondingly numbered tubes.

2-d. Agitate each *4-b tube* gently and allow to stand at room temperature overnight.

3-d. Read: Select the pair of *4-b tubes* (with corresponding numbers) of which the positive member shows complete precipitation of gold and a water-clear supernatant and its negative counterpart shows either no change or at most a slight color change but no precipitation of gold. When two or more pairs of tubes show these changes, from them is selected the pair having the least amount of acetic acid.

Each tube of the selected pair contains the optimal

quantity of 1 per cent acetic acid per ml. of gold solution for this test.

The adjustment of the commercial colloidal gold solution should be made every two weeks.

Method of Performing the Serum Colloidal Gold Test

When the optimal quantity of 1 per cent acetic acid per milliliter of colloidal gold solution has been determined by the above procedure, seven test tubes are set up for each sample of serum to be examined, including a known normal serum and a known positive serum, if available, as a control. Barbital buffer is added to the first six tubes: 0.36 ml. to *tube 1*, and 0.2 ml. to each of *tubes 2* through *6*. Into the seventh tube pipet 0.34 ml. of 1 per cent sodium chloride solution. To *tube 1*, add 0.04 ml. of the serum to be tested; mix the contents; and transfer 0.02 ml. of the mixture to *tube 2*. Then mix the contents of *tube 2* and transfer 0.2 ml. of the mixture to *tube 3*. This procedure is followed through *tube 6*, from which 0.2 ml. of the mixture is discarded. No serum is added to *tube 7*.

The corrected colloidal gold solution is prepared only immediately before it is to be used. Two large test tubes are employed: the required amount of colloidal gold solution is measured into one tube, and the estimated appropriate quantity of acetic acid is delivered to the bottom of the other. The contents of the two tubes are rapidly mixed by pouring the colloidal gold solution into the acid and then pouring that mixture back into the first tube. One ml. of this mixture is then added to each of the above-mentioned seven tubes; the contents of each tube is shaken and allowed to stand at room temperature overnight. The results of the test are then read.

Example. If four samples of serum are to be examined, 28 test tubes and 28 ml. of colloidal gold solution are required. However, to compensate for an expected loss of small amounts of the colloidal gold solution during such procedures as transference, 30 ml. of the solution is prepared. If the optimal quantity of 1 per cent acetic acid solution has been found to be 0.0075 ml. per ml. of gold solution, 0.22 ml. of 1 per cent acetic acid solution is needed: $30 \times 0.0075 = 0.22$. The procedure, as described above, entails delivering 0.22 ml. of acid into one large test tube, and then rather rapidly adding 30 ml. of Lange's colloidal gold solution to it.

Grading of results. Each of the six tubes for each sample of serum is graded on a scale of *5* to *0*, as is standard practice for colloidal gold chloride tests. Complete reduction, *5*, results in colorless supernatant fluid and pronounced precipitation of the colloidal gold; whereas, no reduction, *0*, is indicated by the unchanged red color of the gold solution and no precipitation. The supernatant fluid of the first three tubes of a test with normal serum may show a very slight violet-to-blue color, or no color change at all, the remaining three tubes usually showing no reduction. The seventh tube should show complete reduction of the

gold solution, because of the well-established fact that a ratio of 1.7 to 5 of 1 per cent sodium chloride solution to Lange's colloidal gold solution will completely reduce the latter.

An abnormal serum colloidal gold curve is obtained when there is complete reduction in the first two tubes and at least a slight reduction in the third tube (551000 to 555555), because of elevated gamma globulin. The remaining three tubes usually become progressively nonreactive.

Comment

The above-described methods of adjusting the commercial colloidal gold solution and of performing the test have made the serum colloidal gold test a useful aid in the diagnosis of struma lymphomatosa. The accuracy of evaluation has been increased by comparing results with a control sample of normal serum in which the gamma globulin value is known to be near 0.80 gm. per 100 ml. (normal 0.60 to 0.91 gm. per 100 ml.) as determined by electrophoretic protein analysis. The performance of the test on known normal serum as well as on suspected abnormal serums provides an additional check on the method.

The value of the test is confirmed by the recent report of Skillern and associates[3] which states that of 26 patients having struma lymphomatosa, 22 had an increased level of gamma globulin; and of the 22 patients, 21 had an abnormal serum colloidal gold test. Many other diseases that cause an elevated gamma globulin also will result in an abnormal colloidal gold test. Thus, the value of the test is limited by its nonspecificity and the result should be correlated with other clinical and laboratory findings. The elevation of the serum gamma globulin in struma lymphomatosa was first reported by Fromm and associates.[8a,b]

The pathologic physiology of this increased gamma globulin in struma lymphomatosa is unknown. We at first thought that it might be due to the effects of thyroxine deficiency, but its absence in 80 to 90 per cent of patients with primary hypothyroidism without goiter is somewhat against this, as also suggested by Luxton and Cooke.[6] Owen and McConahey[9] have reported that the abnormal hormone known to be secreted by the thyroid in struma lymphomatosa has all the properties of thyroglobulin. Whether the breakdown of this continuously secreted thyroglobulin is responsible for the elevated gamma globulin is in the realm of further speculation at present.

Summary

An improved method of adjusting commercial colloidal gold solution (Lange's) using known normal and abnormal serums is presented and a modification of the method of performing the serum colloidal gold test is described. The test is a simple, inexpensive diagnostic aid whereby an increase in serum gamma globulin is qualitatively measured. The test in our institution has been useful, but is not as accurate as the more difficult Tiselius electrophoretic serum protein determination as an aid in differential diagnosis of struma lymphomatosa.

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NEURILEMOMAS OF THE LATERAL REGION OF THE NECK

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NEURILEMOMAS of the lateral region of the neck are rare. Five were reported by Stout[1] in 1935 in his series of 52 neurilemomas of peripheral nerves. Since that time only a small number of these tumors has been reported.[2-7] By definition a neurilemoma is a benign neoplasm of the nerve sheath. There has been much controversy about the cellular origin of the tumor, largely because there are two distinct sheaths on peripheral nerves: the sheath of Schwann and the connective tissue sheath. Virchow,[8] in 1863, considered the tumor to be a false neuroma. In 1910 Verocay[9] demonstrated that its origin is in the sheath of Schwann, but applied the inadequate term of *neurinoma*. Mallory[10] and Penfield[11] believed the connective tissue sheath to be the site of origin. Masson[12] supported Verocay's theory, and was able to produce experimentally tumors of the nerve sheath, the origin of which could be traced to Schwann cells. These he therefore termed *schwannomas*. In 1935 Stout[1] introduced the term *neurilemoma*, and in 1940, with Murray,[13] confirmed by tissue culture the origin of these tumors from Schwann cells.

Neurilemomas of the lateral portion of the neck generally present themselves as solitary tumors lying either subcutaneously or deep within the neck. They grow slowly and usually are detected only when they become palpable. Only rarely is pain or tenderness a presenting symptom; such pain results from pressure on adjacent structures and does not originate in the nerve of origin of the tumor. The age and sex of the patient afford no diagnostic help. Neurilemomas vary in diameter from a few millimeters to several centimeters. They may be round, ovoid, or fusiform, and have a smooth or lobulated surface. Grossly, they tend to be firm, discrete, or encapsulated. Often the large tumors are cystic, showing myxomatous degeneration within the lesion. Their color usually is pink, yellowish, or gray, and the cut surface of the tumor is glistening.

Histologically the typical neurilemoma is composed of orderly arranged, long, slender cells with elongated nuclei in a reticulum of long, slender fibers which pass between and parallel to the cells. The cell nuclei tend to lie at the ends of the cells, in palisade formation; this pattern is the so-called *Antoni type A* or *Verocay type*. The *Antoni type B*, or reticular pattern, is characterized by a loosely composed structure with intercellular edema, and vacuoles or microcysts filled with watery fluid. Palisading is absent. Both patterns may be present in the same tumor (Fig. 1). Willis[14] has described a third type of histologic pattern that is essentially epithelioid. The tumor may be grossly cystic (Fig. 2).

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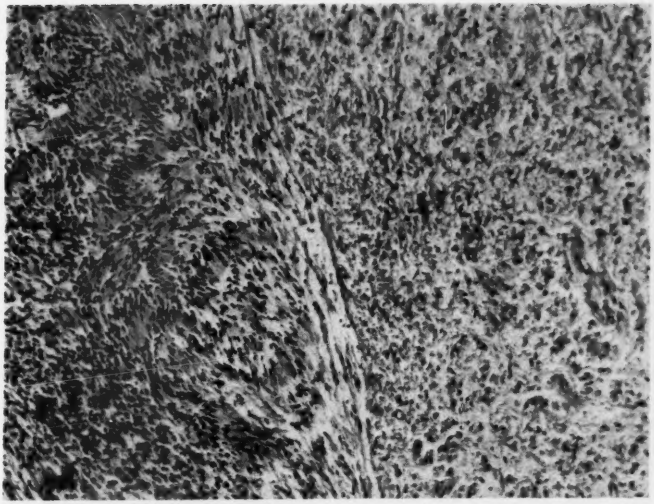

Fig. 1. Microscopic section of a single tumor showing the nuclear palisading of the *Antoni type A* on the left, and the loosely arranged cells without order, *Antoni type B*, on the right; hematoxylin, eosin and methylene blue stain, X85.

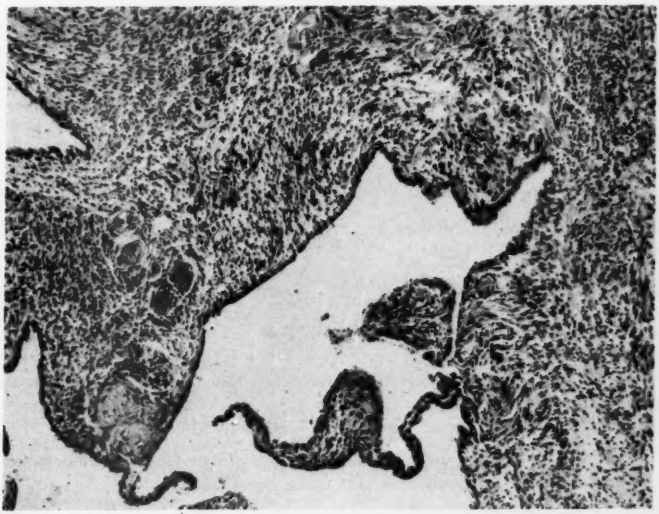

Fig. 2. Cyst formation in neurilemoma; hematoxylin, eosin and methylene blue stain, X100.

Case Reports

Case 1. An 82-year-old man had a large, asymptomatic tumor of the left side of the neck which gradually had increased in size for seven years. On physical examination a firm, rubbery, freely movable mass, 8 cm. in diameter, was noted lying beneath and anterior to the left sternocleidomastoid muscle (Fig. 3). The presumptive clinical diagnosis was branchial cleft cyst.

At operation, the mass was found to be a cystic tumor arising from the vagus nerve 2 cm. below the carotid bifurcation (Fig. 4). A segment of the nerve was removed with the tumor.

Pathologic findings: The lesion was a cystic neurilemoma with a wall 0.5 cm. thick. Microscopic sections showed both Antoni A and B patterns, and cystic areas containing acidophilic granular material.

Case 2. A 38-year-old woman had a presenting complaint of transient pains involving most of the left side of the neck. At the time of onset of the pains, one year prior to examination, she had noticed a mass beneath the angle of the left mandible. This mass subsequently had enlarged slowly. On physical examination a 1.0-cm., slightly tender, freely movable, firm mass was found just below the angle of the left mandible.

At operation, the tumor was excised; no continuity with nerve fibers was noted.

Pathologic findings: The lesion was a neurilemoma, principally Antoni type A with several foci of type B.

Case 3. A 20-year-old woman had a three-year history of generalized peripheral neurofibromatosis. Biopsy of a nodule had shown neurofibroma.

Because of local discomfort, a 1.5-cm. nodule in the right supraclavicular area, diagnosed preoperatively as neurofibroma, was excised.

Pathologic findings: On microscopic examination typical Antoni type B neurilemoma was seen.

Case 4. A 36-year-old woman had the presenting complaint of an asymptomatic lump in the left side of the neck for three weeks. On physical examination, a firm, freely movable tumor, 2 cm. in diameter, was palpated in the left supraclavicular region.

At operation, the tumor was found to be a neurilemoma arising from the brachial plexus. The tumor was removed without damage to the plexus.

Pathologic findings: The tumor was a typical Antoni type A neurilemoma.

Case 5. A 58-year-old woman had had a mixed tumor removed from the left parotid region three years previously. Approximately six months before admission to the Clinic, a mass, presumed to be a recurrent parotid tumor, had been noted deep in the neck beneath the angle of the mandible. On physical examination there was a firm, vaguely outlined, slightly movable, 2-cm. mass deep in the jugulodigastric area.

At operation, a typical neurilemoma was found, arising from an unidentified small nerve close to the pharyngeal wall.

Pathologic findings: Microscopic sections showed neurilemoma, Antoni types A and B, with associated fibrosis and hemorrhage.

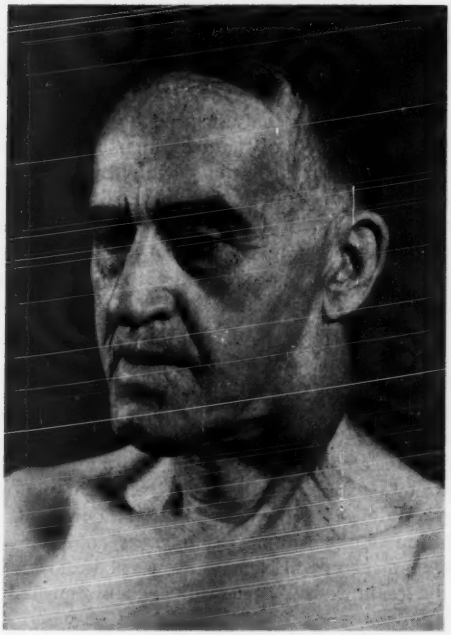

Fig. 3. (Case 1) Patient with large tumor of lateral neck; the mass was freely movable.

Fig. 4. (Case 1) Ovoid and well-encapsulated tumor removed from patient shown in Figure 1. It contained a single large cyst.

Discussion

In all of the above cases, histologic evidence was necessary to make the definitive diagnosis of neurilemoma. In no instance was it the presumptive clinical diagnosis. At best one can only suspect the lesion preoperatively, since any of the discrete lateral tumors of the neck, including tumors of the carotid body, branchial cysts, neoplasms of the parathyroid, lymphoid tumors, and metastases to cervical nodes are equal possibilities. Although in one of our cases (case 3) neurilemoma occurred with von Recklinghausen's disease, this is a rare association.

In the course of examination of the patient with a mass in the lateral cervical region, it is most important to rule out the presence of a growth in the nose, mouth, or throat, which may be the site of origin of a cervical metastasis.

If, at the time of operation, the tumor appears grossly to be a neurilemoma, a biopsy specimen is taken for definitive diagnosis by frozen section. After the diagnosis of neurilemoma has been established, local excision is carried out, with the plane of dissection close to the capsule. If a major nerve trunk is the site of origin, the tumor is dissected free, and the nerve bundles, generally passing to one side of the tumor or spread out over its surface, are preserved. In most instances there is no serious or prolonged functional deficit of residual nerve. If the origin or location of the tumor precludes its complete removal without sacrifice of the nerve, a segmental resection must be performed. Because of the benign nature of the lesion, results after surgical excision usually are good.

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RECENT PUBLICATIONS BY MEMBERS OF THE STAFF

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**Research Department, Department of Clinical Investigation, Ciba Pharmaceutical Products, Inc., Summit, N. J.*

***Fellow in Neurological Surgery.*

†Formerly Fellow in Neurological Surgery.

††Formerly Fellow in Internal Medicine.

KOLFF, W. J., WATSCHINGER, BRUNO*, and VERTES, VICTOR**: Results in patients treated with the coil kidney (disposable dialyzing unit). J.A.M.A. **161**: 1433-1437, Aug. 11, 1956.

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**Formerly Special Fellow in the Division of Research.*

***Resident in Medicine, Mount Sinai Hospital, Cleveland, Ohio.*

ANNOUNCEMENTS

Physician-in-Chief Pro Tempore

Howard P. Lewis, M.D., F.A.C.P., Professor of Medicine, University of Oregon Medical School, will be the sixth annual Physician-in-Chief Pro Tempore on December 13, 14, and 15, 1956. During his tenure, Doctor Lewis will direct the teaching program of the Fellows in Medicine, including ward rounds, lectures, and daily clinics. Members of the medical profession are cordially invited to attend.

Excerpt from SECRETARY'S LETTER—American Medical Association

Letter No. 369

July 18, 1956

"The U.S. Internal Revenue Service has just issued a regulation which is important to physicians.

"Efforts over a long period of time by the A.M.A. Law Department to get the Internal Revenue Service to issue a regulation permitting physicians to deduct their expenditures in taking postgraduate 'refresher' courses have finally paid off.

"The regulation, effective on August 9, provides that expenditures for education are deductible if they are for a 'refresher' or similar type of course taken to maintain the skills directly and immediately required by the physician in his employment or business. An educational course to be covered should be designed for established medical practitioners to help them keep abreast of current developments in the profession; it should be of short duration; it should not be taken on a continuing basis, and should not carry academic credit. Education designed to prepare the practitioner to enter a specialty will not be acceptable.

"When a physician travels away from home primarily to obtain 'refresher' education, his expenditures for travel, meals, and lodging while away from home are deductible. However, expenses for personal activities such as sightseeing, social visiting or entertaining, or other recreation will NOT be allowed."

THE FRANK E. BUNTS EDUCATIONAL INSTITUTE

affiliated with

THE CLEVELAND CLINIC FOUNDATION

announces a postgraduate continuation course in rheumatic diseases on October 24 and 25, 1956

Progress in the Management of Rheumatic Diseases

Tentative Program

Wednesday, October 24, 1956

Morning Session . . . . . ARTHUR L. SCHERBEL, M.D., *Presiding*

8:00- 9:00 a.m.	.	Registration
9:00- 9:15 a.m.	.	Introductory Remarks . . . . . CHARLES L. LEEDHAM, M.D.
9:15- 9:35 a.m.	.	Dermatomyositis . . . . . GEORGE H. CURTIS, M.D.
9:35- 9:55 a.m.	.	Diagnosis and Treatment of Septic Intervertebral Disc . . . . . W. JAMES GARDNER, M.D.
9:55-10:15 a.m.	.	Natural History of Rheumatoid Arthritis . . . . . WILLIAM D. ROBINSON, M.D. *
10:15-10:35 a.m.	.	Modern Concepts of Lupus Erythematosus . . . . . JOHN R. HASERICK, M.D.
10:35-10:50 a.m.	.	Coffee Break
10:50-11:10 a.m.	.	Histopathologic and Clinical Manifestations of Angiitis . . . . . S. L. SCHUCHTER, M.D.
11:10-11:30 a.m.	.	Pathologic Changes in Certain of the So-Called Collagen Diseases . . . . . JOHN B. HAZARD, M.D.
11:30-12:00 noon	.	Symposium: Early Diagnosis of Collagen Disease *Moderator*—ARTHUR L. SCHERBEL, M.D. GEORGE H. CURTIS, M.D. JOHN R. HASERICK, M.D. JOHN B. HAZARD, M.D. WILLIAM D. ROBINSON, M.D. *
12:30- 1:30 p.m.	.	Luncheon—*Courtesy of Bunts Institute*

Afternoon Session WILLIAM D. ROBINSON, M.D., * *Presiding*

2:00- 2:20 p.m.	.	Diagnostic Laboratory Procedures in Rheumatoid Arthritis . . . . . WILLIAM S. CLARK, M.D. *
2:20- 2:40 p.m.	.	Physical Therapy in Rheumatoid Arthritis . PAUL A. NELSON, M.D.
2:40- 3:00 p.m.	.	Chemotherapy in Rheumatoid Arthritis: A Concept . . . . . ARTHUR L. SCHERBEL, M.D.

**Guest speaker.*

3:00- 3:20 p.m.	Surgery in Advanced Joint Diseases	ALFRED W. HUMPHRIES, M.D.
3:20- 3:35 p.m.	Coffee Break	
3:35- 3:55 p.m.	Diagnosis and Treatment of the Painful Shoulder	J. I. KENDRICK, M.D.
3:55: 4:15 p.m.	Tension Fibrositis	LEONARD L. LOVSHIN, M.D.
4:15- 4:35 p.m.	Clinical Manifestations of Pulmonary Hypertrophic Osteoarthropathy	DONALD B. EFFLER, M.D.
4:35: 5:05 p.m.	Symposium: Management of Rheumatoid Arthritis and Related Disorders	*Moderator*—ARTHUR L. SCHERBEL, M.D. JOHN R. HASERICK, M.D. ALFRED W. HUMPHRIES, M.D. PAUL A. NELSON, M.D. WILLIAM D. ROBINSON, M.D. * PENN G. SKILLERN, M.D.

Thursday, October 25, 1956

Morning Session . . . . . ARTHUR L. SCHERBEL, M.D., *Presiding*

9:00- 9:20 a.m.	Acute Rheumatic Fever	ROBERT D. MERCER, M.D.
9:20- 9:40 a.m.	Rheumatic Heart Disease	RICHARD N. WESTCOTT, M.D.
9:40-10:00 a.m.	Surgery in Rheumatic Heart Disease	LAURENCE K. GROVES, M.D.
10:00-10:20 a.m.	Coffee Break	
10:20-10:40 a.m.	Management of Acute and Chronic Gouty Arthritis	WILLIAM D. ROBINSON, M.D. *
10:40-11:00 a.m.	The Carpal Tunnel Syndrome	GEORGE S. PHALEN, M.D.
11:00-11:20 a.m.	Management of Osteoarthritis	SALVATORE R. LATONA, M.D. *
11:20-12:10 p.m.	Presentation of Cases	
12:10-12:30 p.m.	Questions and Answers	

Affiliations of Guest Speakers

WILLIAM S. CLARK, M.D., Assistant Professor of Medicine, Western Reserve University School of Medicine, Cleveland, Ohio.

SALVATORE R. LATONA, M.D., Assistant in Medicine, University of Buffalo School of Medicine, Buffalo, New York.

WILLIAM D. ROBINSON, M.D., Professor of Medicine, University of Michigan Medical School, Ann Arbor, Michigan; President of the American Rheumatism Association.

**Guest speaker.*

REGISTRATION FORM

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2020 East 93 Street
Cleveland 6, Ohio

Please register me for the course *Progress in the Management of Rheumatic Diseases*, to be given October 24 and 25, 1956. (Registration fee is $15.00, except for interns and residents, and members of the Armed Forces in uniform, who will be admitted free.)

I am enclosing a check for $5.00 and will pay the remainder on October 24. (Please make check payable to The Frank E. Bunts Educational Institute.)

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Name of Medical School and
Date of Graduation . . . . . .

(*This course is open only to graduates of approved medical schools.*)

THE FRANK E. BUNTS EDUCATIONAL INSTITUTE

affiliated with

THE CLEVELAND CLINIC FOUNDATION

announces a postgraduate continuation course in blood bank management on November 15 and 16, 1956

Blood Bank Methodology

Tentative Program

Thursday, November 15, 1956

Morning Session		CHARLES L. LEEDHAM, M.D., *Presiding*
8:00- 9:00 a.m.	Registration	
9:00- 9:15 a.m.	Introductory Remarks	CHARLES L. LEEDHAM, M.D.
9:15- 9:35 a.m.	Historical Aspects of Blood Transfusions	ALEXANDER T. BUNTS, M.D.
9:35- 9:55 a.m.	Laboratory Follow-Up on Transfusion Reactions	JOHN W. KING, M.D.
9:55-10:15 a.m.	Clotting Factors in Bank Blood	WILLIAM A. HAWK, M.D.
10:15-10:30 a.m.	Blood Volume Determinations as an Aid in Determining Blood Needs	CARL E. WASMUTH, M.D.
10:30-10:50 a.m.	Coffee Break	
10:50-11:30 a.m.	Quantitative Hemaglutination Studies in the A-Anti-A System	LT. COL. JOSEPH AKEROYD, MSC, USA*
11:30-12:15 p.m.	Panel Discussion	*Moderator*, LT. COL. JOSEPH AKEROYD, MSC, USA* WILLIAM A. HAWK, M.D. JOHN W. KING, M.D. NORMA J. LYONS, M.T. (A.S.C.P.) CARL E. WASMUTH, M.D.
12:30- 2:00 p.m.	Luncheon—*Courtesy of Bunts Institute*	
Afternoon Session		JOHN W. KING, PH.D., M.D., *Presiding*
2:00- 2:15 p.m.	Transfusions in Blood Dyscrasias	JOHN D. BATTLE, JR., M.D.
2:15- 2:30 p.m.	Blood Transfusion Problems During Anesthesia	DONALD E. HALE, M.D.
2:30- 3:20 p.m.	Blood Group Genetics	ROGER W. MARSTERS, PH.D.*
3:20- 3:35 p.m.	Coffee Break	
3:35- 3:55 p.m.	Exchange Transfusions in Pediatric Practice	ROBERT W. MERCER, M.D.
3:55- 4:15 p.m.	Chemical Tests for the Screening of Blood Donors	ADRIAN HAINLINE, JR., PH.D.

*Guest speaker.

4:15- 4:45 p.m. . Panel Discussion . . . . . *Moderator*, ROGER W. MARSTERS, PH.D.*
JOHN D. BATTLE, JR., M.D.
ADRIAN HAINLINE, JR., PH.D.
DONALD E. HALE, M.D.
ROBERT W. MERCER, M.D.

Friday, November 16, 1956

Morning Session . . . . . JOHN W. KING, PH.D., M.D., *Presiding*

9:00- 9:15 a.m. . Problems in Multiple Transfusions. . . . . JOHN W. KING, M.D.

9:15-10:00 a.m. . Current Concepts in Blood Banking . . . . . LT. COL. JOSEPH AKEROYD, MSC, USA*

10:00-10:20 a.m. . Coffee Break

10:20-10:40 a.m. . Hemoglobinuric Nephrosis . . . LAWRENCE J. MCCORMACK, M.D.

10:40-11:00 a.m. . Allergic Problem in Blood Transfusion Reactions . . . . . RICHARD R. EVANS, M.D.

11:00-11:35 a.m. . Transfusion Problems in the Use of the Heart Pumps and the Artificial Kidney . . . . . WILLEM J. KOLFF, M.D.

11:35-11:50 a.m. . Current Experience with D^u. . . . . ROGER W. MARSTERS, PH.D.*

11:50-12:30 p.m. . Panel Discussion. *Moderator*, LT. COL. JOSEPH AKEROYD, MSC, USA*
RICHARD R. EVANS, M.D.
JOHN W. KING, M.D.
WILLEM J. KOLFF, M.D.
ROGER W. MARSTERS, PH.D.*
LAWRENCE J. MCCORMACK, M.D.

Afternoon Session

2:00 p.m. . . . . .Tour of the Blood Bank and the Clinical Pathology Laboratories Conducted by Doctor King and Miss Lyons.

5:10 p.m. . . . . .Open meeting sponsored by The Frank E. Bunts Educational Institute and the Cleveland Society of Medical Technicians.
Recent Advances in Blood Bank Technic . . . . . LT. COL. JOSEPH AKEROYD, MSC, USA*

Affiliations of Guest Speakers

LT. COL. JOSEPH AKEROYD, MSC, USA, Assistant Chief, Hematology Department, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D.C.

ROGER W. MARSTERS, PH.D., Assistant Professor of Clinical Biochemistry, Western Reserve University School of Medicine; Clinical Pathologist in Charge of Blood Bank, City Hospital, Cleveland, Ohio.

The Registrar of the Bunts Institute now is accepting reservations for the course which is limited to 125 registrants. (Please see registration form on page 288.)

**Guest speaker.*

REGISTRATION FORM

THE REGISTRAR
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